IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re of Application of: **Jeremy I. Levin, et al.**

Serial No.: Group No.:

Confirmation No: Customer No. **25291**

Filed: Examiner:

For: **ALKYNYL CONTAINING HYDROXAMIC ACID COMPOUNDS AS MATRIX METALLOPROTEINASE/TACE INHIBITORS**

Commissioner for Patents
Washington, DC 20231

PRELIMINARY AMENDMENT

Sir:

Preliminary to the examination of the present application please amend the application as follows.

IN THE SPECIFICATION

Please replace the paragraph beginning on page 1, line 4, with the following:
--This is a divisional of copending application serial no. 09/492,686 filed on January 27, 2000, which application claims the benefit of U.S. Provisional Application No. 60/155,184 filed January 27, 1999, the entire disclosure of each being hereby incorporated by reference.--

CERTIFICATION UNDER 37 CFR §1.10

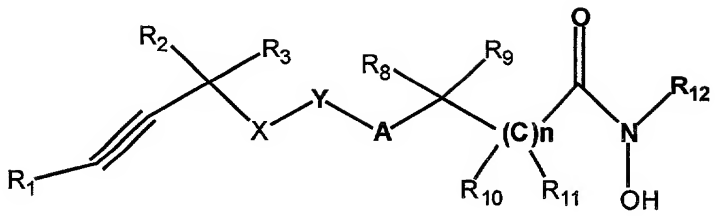
I hereby certify that this paper and the documents referred to as enclosed therein are being deposited with the United States Postal Service on the date written below in an envelope as "Express Mail Post Office to Addressee" Mailing Label Number EL909159916US addressed to the Commissioner for Patents, Washington, DC 20231.

12-21-01
Date

Regina Benson
Regina Benson

In the Claims

1. A compound of formula



I

wherein:

R_1 is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C4-C8-cycloheteroalkyl;

R_2 and R_3 are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH;

R_7 is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)-R_1, -SO_2-R_1, -C(O)-NHR_1, -C(O)NR_5R_6, -C(O)$R_1NR_5R_6$, -C(O)-OR_1, -C(NH)-NH_2.

R_8, R_9, R_{10}, and R_{11} are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R8 and R9, R9 and R10 or R10 and R11, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C4-C8-cycloheteroalkyl ring;

R_{12} is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;

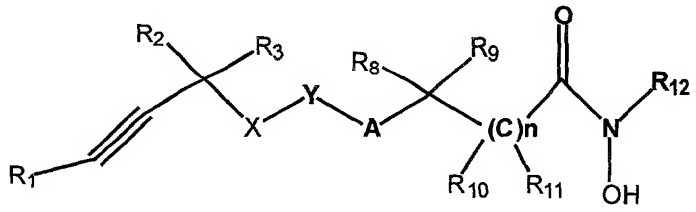
A is O, S, SO, SO_2, NR_7, or CH_2;

X is O, S, SO, SO_2, NR_7, or CH_2;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R_8 and R_9 together with the carbon atom to which they are attached may not form a piperdinyl or tetrahydropyranyl ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

4. A method of inhibiting pathological changes mediated by TNF-α converting enzyme (TACE) in a mammal in need thereof which comprises administering to said mammal a therapeutically effective amount of a compound having the formula



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R_8, R_9, R_{10}, and R_{11} are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R8 and R9, R9 and R10 or R10 and R11, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C4-C8-cycloheteroalkyl ring;

R_{12} is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;

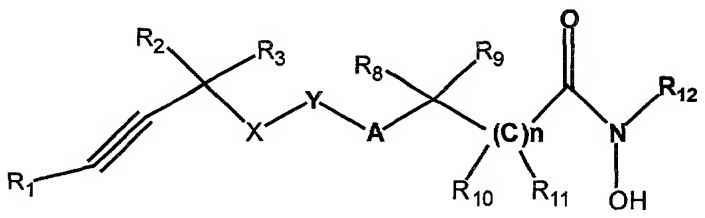
A is O, S, SO, SO_2, NR_7, or CH_2;

X is O, S, SO, SO_2, NR_7, or CH_2;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R_8 and R_9 together with the carbon atom to which they are attached may not form a piperdinyl or tetrahydropyranyl ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

6. A pharmaceutical composition comprising a compound having the formula



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R_8, R_9, R_{10}, and R_{11} are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R8 and R9, R9 and R10 or R10 and R11, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C4-C8-cycloheteroalkyl ring;

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X is O, S, SO, SO_2, NR_7, or CH_2;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R_8 and R_9 together with the carbon atom to which they are attached may not form a piperdinyl or tetrahydropyranyl ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

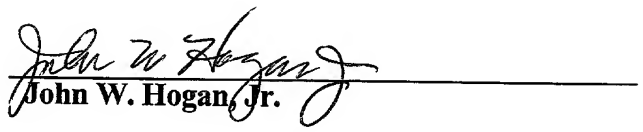
Please cancel claim 3, without prejudice.

REMARKS

The present application is a divisional of 09/492,686. The specification has been amended to reflect the complete prosecution history. The claims have been amended to delete subject matter which has been allowed in the parent application.

Attached hereto is a marked-up version of the changes made to the application by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made."

Applicants believe that the present application is in condition for allowance and respectfully request that the Examiner enter the amendment and allow the application. Favorable treatment of the application is earnestly solicited.



John W. Hogan, Jr.

Reg. No. **32,703**

American Home Products Corporation
Patent Law Department
Five Giralda Farms
Madison, NJ 07940
Tel. No. (973) 683-**2152**

Version with Markings to Show Changes Made

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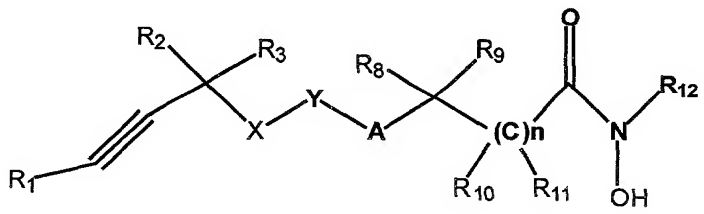

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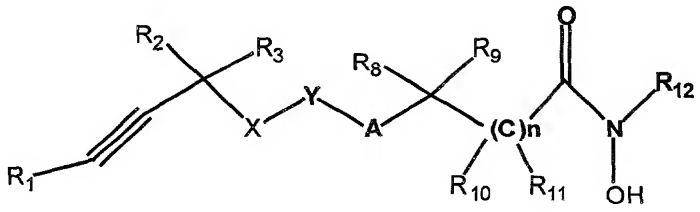

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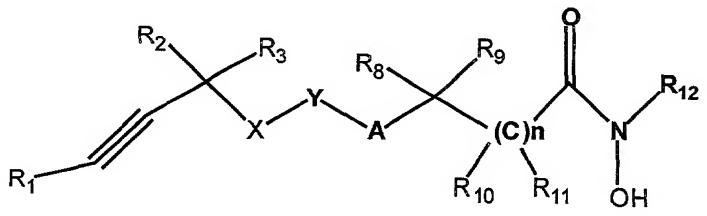

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